Chapter 46

Intravascular Laser Irradiation of Blood

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46.1 Introduction

Intravascular laser irradiation of blood (ILIB) is a systemic low-level laser modality that aims the irradiation of blood. Discovered by Russian scientists in the 1970s, ILIB consists of laser blood irradiation through a fiber optic inserted in a vascular channel, usually a vein in the forearm. ILIB irradiation lasts for about 30 min, which is assumed to be sufficient time for the whole blood to receive light, enabling systemic effect. Thus, blood components such as blood lipids, platelets, immune system, and red cells are the main targets.

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Although the mechanisms of ILIB are uncertain and need to be assessed by further randomized controlled trials and clinical reports, many studies from Russia show favorable effects of the technique. ILIB has been studied for a wide range of medical conditions, including diabetes mellitus, asthma, chronic hepatitis, multiple sclerosis, cardiovascular diseases, hypertension, and autoimmune diseases [1–6].

In this chapter, a summary of the main indications and effects of ILIB will be presented in order to introduce this promising "new" treatment modality, stimulate new researches on the mechanisms of action, and propose that further randomized clinical studies are recommended. Still, new forms of noninvasive systemic irradiation have already been developed and appear to be promising, such as modified and intranasal ILIB techniques.

46.2 History of ILIB

In the 1970s, the Russians began research on ILIB with helium–neon (He–Ne) laser, at 632.8 nm of wavelength, based on the works of Mester et al. [6]. Originally this method was developed for the treatment of cardiovascular diseases. Further, improvements in blood's rheological properties and microcirculation as well as reduction in the infarction area have been proved. Basic research on the mechanisms of action of ILIB has also significantly increased, showing the antioxidant effect of ILIB therapy by the reactivation of superoxide dismutase (SOD) enzyme [7]. SOD is a key enzyme that controls the levels of free radicals and leads to hemostasis and to prevent many systemic diseases.

The first laser used was the He–Ne laser (632.8 nm), with a power of 1–3 mW and a period of exposure of 20–60 min. The technique involves inserting an intravenous catheter in one of the upper limbs, coupled to an optical fiber that radiates blood with laser directly and continuously at the application site, distributing that irradiated blood through the circulation throughout the body (Fig. 46.1). Usually, the treatments are carried out once or twice a day up to 10 appointments in all.

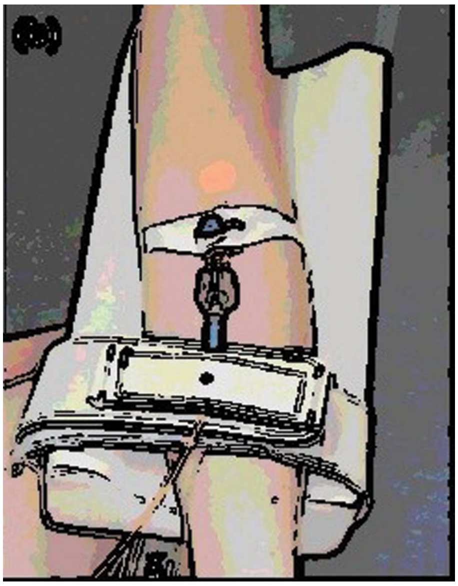

Figure 46.1 Intravenous laser irradiation of blood.

Most of the Russian studies published since the 1970s using the ILIB technique were little known in the West because of decades of political separation and were, therefore, regarded with disapproval. Thus, ILIB remained into discredit for decades due to the lack of scientific evidence on the mechanisms of action of laser therapy. At that time, laser therapy was very unclear and empirical, and only the group of the cell biologist Tina Karu was studying the mechanisms.

Currently, new studies and clinical findings published in Russian magazines have contributed to the permanence of ILIB and instigated more scientists to carry out research. Many Western studies of great scientific importance have brought a better understanding of the mechanisms of action of laser therapy and elucidated many of the effects previously reported by the Russians [7, 8].

Among the mechanisms of action known today, we will highlight light action on cell membrane, a mechanism that may explain the activation of immune cells, mast cell degranulation, and modulation of lipids and other blood components; light shutdown of nitric oxide (NO) from hemoglobin, improving oxygenation of the blood and vasodilatation; cell biostimulation by light absorption of mitochondrial enzymes (mainly cytochrome c oxidase), reactivating the cellular metabolism (ATP, reactive oxygen species [ROS], tumor necrosis factor-α [TNF-α]) and acting on red and endothelial cells; the induction of an electric field, polarizing blood substances to the center of the vessel and temporarily increasing blood flow [9]; and finally, the reactivation of endogenous SOD enzyme [7], an antioxidant activity that is important in preventing many systemic diseases. It is believed that the SOD effect is the main mechanism of action of ILIB; therefore, this technique is also claimed to be an antioxidant and anti-aging therapy.

46.3 Antioxidant Action of ILIB

In our body, cells produce free radicals during the oxygen combustion process that converts the nutrients absorbed from food into energy. External factors may also contribute to the increased formation of these molecules: environmental pollution; X-ray and ultraviolet radiation; cigarette; alcohol; pesticide residues; substances present in foods and beverages (chemical additives, preservatives, hormones); stress; consumption of saturated fats and consumption of animal fat.

The interaction of free radicals with the biological system, regardless of their source, can result in significant health consequences, contributing to the development of certain pathologies such as aging, Parkinson's disease, cancer, arthritis, cardiovascular and cardiorespiratory complications, among others.

To combat the damaging effects of free radicals, the body uses its defense system. The enzyme system is the main way of combating free radicals, which prevents their formation or neutralizes them. Among the enzymes involved in the enzymatic defense system, SOD plays the primary role. SOD inhibits the superoxide ion, which is the first free radical formed from molecular oxygen and serves as a substrate for triggering the formation of more harmful radicals such as hydroxyl (OH).

Table 46.1 General effects of ILIB demonstrated in the literature

ILIB Effects	Literature
Regulation of blood lipids	Lebed'kov et al. [10]; Poluéktova et al. [11]; Huang et al. [12]; Babaev et al. [13]
Normalizing action on lipid peroxidation	Azbel et al. [14]; Safafov et al. [15]; Karneev et al. [16]
Inhibition of platelets aggregation (lessening the likelihood of clot formation)	Sirenko et al. [17]; Prokopova et al. [18]; Shval'b et al. [19]; Brill et al. [20]
Activated platelet aggregation	Paleev et al. [21]; Gao et al. [22]
Activation of immune system (dendritic cells, macrophages, and lymphocytes)	Dmitriev et al. [23]; Kupnovyts'ka [24]; Palćhun et al. [25]; Koshelev and Chalyk [26]; Hanul et al. [27]; Stupak and Rodiukova [28]
Immunomodulation	Dedenko [29]; Marchuk and Kuzmich [30]; Alizade and Karaeva [31]; Sidorov et al. [32]; Tsvettsikh et al. [33]; Shakhova et al. [5]; Chiran et al. [34]
Interference in the arachidonic acid cascade/anti-inflammatory effects	Tsuman et al. [35]; Sidorov et al. [32]; Polosukhin [36]; Burduli and Krifaridi [37]; Shakhova et al. [5]
Normalize hemostasis system	Koshelev and Chalyk [26]
Antioxidant defense	Dedenko [29]; Grigor'eva et al. [38]; Koshelev and Chalyk [26]; Zubkova et al. [39]; Koshelev and Chalyk [26]; Tsvettsikh et al. [33]; Vladimirov et al. [7]; Huang et al. [12]; Farkhutdinov [40]; Karneev et al. [16]; Arnall et al. [41]; Burduli and Krifaridi [42]; Burduli and Aleksandrova [3]; Shakhova et al. [5]; Burduli and Balaian [43]
Vasodilatation	Sirenko et al. [17]; Alizade and Karaeva [31]; Alizade and Karaeva [44]
Improves rheological blood characteristics, reduces erythrocyte sedimentation and blood viscosity	Dedenko [29]; Prokopova et al. [18]; Alizade and Karaeva [31]; Paleev et al. [21]; Palćhun et al. [25]; Alizade and Karaeva [44]; Siposan and Lukacs [45]; Mi et al. [46]; Iaitskiĭ et al. [47]; Sarycheva et al. [4]; Simonenko et al. [48]
Increasing in microcirculation	Kirsanova et al. [49]; Iakubenia et al. [50]; Burduli and Gazdanova [51]; Burduli and Gutnova [52]; Burduli and Tadtaeva [53]; Shakhova et al. [5]

SOD is the fifth most abundant enzyme in the body. But in some pathological conditions, the enzyme can be inactivated, as in blood acid conditions, inflammatory situation, and chronic diseases. Laser radiation of inactive SOD has been proved to reactivate the enzyme, even at acidic pH conditions in which inactivation occurs in pathological situations [7]. Thus, ILIB can reverse the oxidative stress present in various diseases.

Treatment with ILIB is aimed at treating the patient for functional recovery of the antioxidant enzyme system, balancing the individual as a whole, to provide a functional optimization of each system.

The effects of ILIB and diseases treated by the ILIB technique are summarized in Tables 46.1 and 46.2, respectively.

Table 46.2 Clinical effects of ILIB

Diseases	Clinical Effects of ILIB	Literature
Arthritis	• Reduction in the rheumatoid blood factor to 1:20 titers • No side effects or complications • Reduction in the time of patients' stay at hospital • Anti-inflammatory and immunomodulating action in patients with rheumatoid arthritis • Normalization of titer of IgA and IgG levels • Synergistic anti-inflammatory effect of ILBI in combination with tocilizumab	Tupikin 1985 [54], Sidorov et al. [32], Chiran et al. [34]
Asthma	• Retained free radical oxidation defects and the disease symptoms • Better morphofunctional parameters of red blood cells	Farkhutdinov [40], Sarycheva et al. [4]
Atherosclerosis	• Better results in morphofunctional state of erythrocytes and hemorheology • ILIB therapeutic effect persisted during 3 months in most patients	Iaitskiĭ et al. [47]
Acute period of hemorrhagic shock and after resuscitation	• Improvement in circulation, gas exchange in lungs, and tissue perfusion • Activation of regulatory mechanisms of the regional blood flow redistribution	Kirsanova et al. [49]
Bronchitis	• Positive effect on circulatory system by changing hyperkinetic hemodynamics into normokinetic one	Burduli and Aksenova [55]
Chronic brain ischemia	• Normalizing action on lipid peroxidation and antioxidant defense	Karneev et al. [16]

Table 46.2 (*Contd.*)

Diseases	Clinical Effects of ILIB	Literature
Chronic hepatitis and reactive hepatitis	• Reduction in the functional activity of thrombocytes in the presence of fibrinogen and adrenaline hydrochloride • Improvement in endothelium function • Compensation of NO deficit • Protection of the organism against free radicals decreases severity of oxidative stress • Normalization in the plasma nitric oxide level • Marked beneficial effect on the cytokine system	Spasov et al. [1], Burduli and Krifaridi [42], Burduli and Krifaridi [37]
Chronic venous insufficiency	• Hypocoagulation, lower hematocrit index	Shval'b et al. [19]
Diabetic angiopathies	• Decrease in the activity of free radical oxidation • Action on antiperoxide protection enzymes • Improvement on issue microcirculation	Grigor'eva et al. [38]
Diabetes	• Impact on the blood lipid and phospholipid components and erythrocyte membrane • Favorably affects the blood components • Hypolipedemic and hypoglycemic effects • Decreased concentration of NO in the blood • Improves peripheral protective sensation in patients by a mechanism other than an increased NO production	Lebed'kov et al. [10], Poluéktova et al. [11], Arnall et al. [41]
Coronary heart disease	• Changes in erythrocyte number • Effects on the blood antioxidative system • Increase in microcirculation • Increase in endothelial oscillations and capillary blood flow • Increase in endothelial functional activity • Decrease in membrane toxicity by 43% • Decrease in the activity of blood serum components • Significant decrease in the levels of total cholesterol, and low-density lipoproteins • Increase in the content of high-density lipoproteins • Alleviation of pain syndrome • Reduction in ventricular arrhythmias frequencies, heart failures, condition recurrences, and mortality rate • Reduction in the hypophyseoadrenocortical and aldosteron-renin-angiotensin system activities	Simonenko et al. [48], Zubkova et al. [39], Burduli and Gazdanova [51], Azbel et al. 1993 [14], Diasamidze 2004 [56], Sirenko et al. 1990 [17]

(*Contd.*)

Table 46.2 (*Contd.*)

Diseases	Clinical Effects of ILIB	Literature
	• Reduction in blood levels of dilatants and proaggregants (PGF2 alpha, vasopressin, angiotensin II) • Increase in vasodilating and antiaggregation hormones (PGE, PGI2) levels • Improvement in PGI2/TxB2 ratio	
Ischemic heart disease	• Increase in the activity of ATP-ase • Index of erythrocyte deformability • Improvement in cardiac function • Optimization of the structural, functional organization of the cellular membrane	Vasil'ev et al. [57]
Esophageal cancer	• Immunorehabilitation effect • Lower postoperative complications rate • Mortality reduction • Improvement in three-year survival rate indexes	Hanul et al. [27]
Gastro-esophageal reflux disease	• Increase in PGE2 to the levels typical of those in healthy individuals • Significant decrease in all esophageal pH-metry parameters • The DeMeester score achieved normal values • All quality-of-life indicators, except for physical function index, significantly improved • Elevation of pro-inflammatory prostaglandin levels and the improvement of parameters of microcirculation • Normalization of plasma levels of stable nitric oxide metabolites regardless of their initial value, either high or low	Burduli and Tadtaeva [53], Burduli and Tadtaeva [58], Burduli and Balaian [43]
Hypertension	• Drop in the arterial blood pressure • Improvement in general condition of patients • Enhancement of the effectiveness of antihypertensive preparations • Favorable shifts in immunological and hemorheological indices • Beneficial clinical effect for up to 4–8 months • Drop of arterial pressure • Improvement in viscous and elastic properties of blood and its hemodynamic index • Significant decrease in Willebrand factor activity • Normalization of the NO level regardless of its initial value	Alizade and Karaeva [31], Alizade and Karaeva [44], Burduli and Aleksandrova [3]

Table 46.2 (*Contd.*)

Diseases	Clinical Effects of ILIB	Literature
Liver problems	• Alleviation of major clinical symptoms • Significant positive changes in biochemical parameters (AST, ALT, bilirubin, alkaline phosphatase, lactate dehydrogenase, and total cholesterol)	Babaev et al. [13]
Pancreatitis	• Recovery of lymphocyte activity • Increase in the ATP content in erythrocytes • Inhibition of blood proteolytic activity • Enhancement of free radical oxidation, kallikrein–kinin system activity, blood oxygen transport • Correction of endotoxic pancreatogenic syndrome • Positive shifts in the immunological status, morphofunctional characteristics of the red blood cells and hemoglobin, hepatic and renal functions • Improvement in microcirculation regardless of its hemodynamic type • Normalization of ceruloplasmin content in the plasma • Avoids infection of pancreatic lesions in 67.7% • Decrease in lethality rate of sterile pancreonecrosis from 24.4% to 5.1% and of infected pancreonecrosis from 42.8% to 23.1%	Dmitriev et al. [23], Dedenko [29], Burduli and Gutnova [52], Burduli and Gutnova [59], Geĭnits et al. [60]
Pneumonia	• Positive dynamics in microcirculation in addition to conventional medication • Pronounced effects on blood rheological characteristics: reduced blood viscosity, improved viscoelastic properties and osmotic resistance of erythrocytes • Decrease in blood viscosity • Hypocoagulative effect of intravascular • Normalization of clinico-roentgenologic	Burduli and Pilieva [61], Paleev et al. [21], Prokopova et al. [18]
Psoríasis	• Increased levels of anti-inflammatory cytokines • Decreased levels of pro-inflammatory cytokines • Immunomodulatory effect • Stimulates the antioxidative system • Improves microcirculation	Shakhova et al. [5]
Parkinson's disease	• Reduction in neurological deficit • Normalization of the activity of MAO B, Cu/Zn-SOD, and immune indices • Correlation between humoral immunity and activity of the antioxidant enzymes (SOD, catalase) • Interaction between blood cells	Komel'kova et al. 2004 [62], Vitreshchak et al. 2003 [63]

(*Contd.*)

Table 46.2 (*Contd.*)

Diseases	Clinical Effects of ILIB	Literature
Pyelonephritis	• Stimulates the antioxidant system, in particular, the activity of superoxide dismutase • Immunomodulation effect • Changes in beta 2-microglobulin, lipid peroxidation, middle-size molecules in blood and urine • Effective treatment of acute calculous pyelonephritis	Tsvettsikh et al. 1999 [33], Safafov et al. [15]
Refractory tachyarrhythmias	• Effect on the neurohumoral regulation, normalization of barrier, and receptor function of myocardium cell membranes • Overcomes refractivity of tachyarrhythmias to antiarrhythmic agents	Kupnovyts'ka [24]
Septic complications in otorhinolaryngology	• Activation of immune system • Improvement in rheological blood characteristics • Enhancement of tissue regeneration • Immunostimulating effect	Palchun et al. [25]
Spinal cord injury	• Higher mitochondrial DNA (mtDNA) copy number • Higher white blood cell adenosine triphosphate (WBC ATP) synthesis • Higher total antioxidant capacity (TAC) with significantly reduced malondialdehyde (MDA) • Reduction in low-density lipoprotein (LDL) • Significant increase in high-density lipoprotein (HDL) • Alleviation of oxidative stress and mitochondrial dysfunction	Stupak and Rodiukova 1999 [28], Huang et al. 2012 [12]
Suppurative lung diseases	• More rapid normalization of the indices of morphologic composition of gases and acid–base state of blood • Immunologic status of the organism, functions of external respiration • Incidence of postoperative complications reduced by 4% • Duration of hospital stay shortened by 8.1 days	Marchuk and Kuzmich [30]

Table 46.2 (*Contd.*)

Diseases	Clinical Effects of ILIB	Literature
Suppurative peritonitis	• Stimulates the bone marrow and organs in which blood elements are stored • Increase in cell number of intermediate • Reduction in the number of prehemolytic and degenerating forms of red cells in various stages of peritonitis • Retransformation of stomatocytes into discocytes, but no marked effect on echinocytic transformation	Zimon et al. [64]
Traumatic abdominal organs injuries	• Improvement in the results of conventional treatment and reduction in complications rate • Boosts functional activity of leucocytes • Normalization of hemostasis system • Antioxidant defense	Koshelev and Chalyk [26]
Tuberculosis	• Promotion of pulmonary vascular tone • Better microcirculatory blood flow • Increased pulse blood filling in the affected portion of the lung • Enhancement of the conventional treatment efficiency • Accelerated positive changes of tuberculosis by 2.5–3.5 months • Smooth course of tuberculosis developing less pronounced residual changes in the lung	Iakubenia et al. [50], Rusakova et al. [65]
Infectious, destructive lung diseases	• Reversion of the inflammatory process • Stabilization of fibroplastic processes	Polosukhin [36]

46.4 Modified ILIB Techniques

The original ILIB technique introduced by the Russians presents a big disadvantage: invasive irradiation. Recently, Chinese literature and clinical practice in Brazil have suggested other forms of systemic, noninvasive irradiation, such as intranasal laser irradiation and skin irradiation performed on the wrist. This modification in the irradiation technique allows more frequent use and expands its applicability to home care treatment.

46.4.1 *Intranasal Irradiation*

Since 1989 many Russian groups have studied the therapeutic effects of intranasal laser photobiomodulation (ILPBM) on the local inflammation in vasomotor rhinitis [66]. In the mainland of China, ILPBM has been studied for the treatment of internal diseases. The special treatment began in 1998 and was called intranasal low-intensity laser therapy (ILILT).

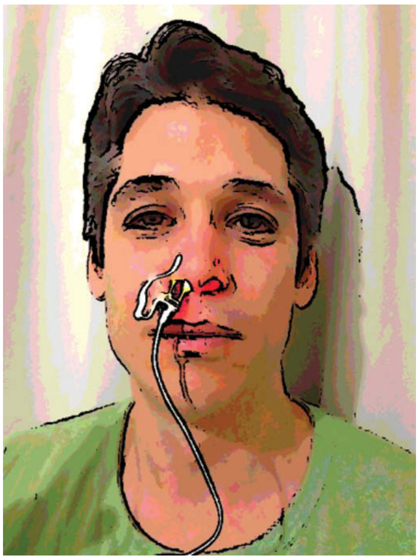

Figure 46.2 Intranasal laser irradiation.

The technique involves a diode laser device (mainly 650–660 nm) with 10–30 mW of power, attached inside the nose (Fig. 46.2). The treatment protocol varies from 15 min to 30 min per day for 10 days (consecutively or not). There are four suggested pathways mediating the ILILT: olfactory nerves, blood cells, meridians in traditional Chinese medicine, and autonomic nervous system. ILILT has been applied to treat cerebral injury [67], allergic rhinitis [68], blood stasis syndrome of coronary heart disease, myocardial infarction, and brain diseases such as insomnia, intractable headache, Alzheimer's disease, diabetic peripheral neuropathy, and acute ischemic cerebrovascular disease [69].

46.4.2 *Wrist Skin Irradiation*

With the advancement of technology, more powerful diode lasers appeared on the market. This contributed to the noninvasive idea (introduced by Brazilian researches a few years ago) of irradiating the skin on the wrist to reach blood vessels. The idea was supported by the local industry, which developed a special device for this modified ILIB (MILIB) technique (Fig. 46.3). This technique and its benefits became known to health professionals and patients. Among the advantages of the traditional ILIB technique include improvement in sleep quality and emotional state, increased performance in sports, and enhanced physical and mental disposition in general. These effects, however, have not been published yet.

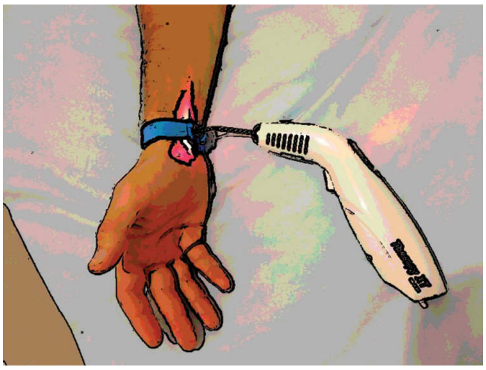

Figure 46.3 Wrist skin laser irradiation (modified ILIB).

The MILIB technique involves a red (660 nm) diode low-level laser, with a power of 60–100 mW. The laser optical fiber is placed on the skin of the wrist region (acupuncture point region lung 8), secured with an elastic band. The irradiation is performed for 30 min continuously, and the dosage is varied from once a week for 10 weeks to daily application for 10 days depending on the type of disease.

All these new ILIB techniques need to be better studied and researched. Further investigations on the irradiation time, amount of light, and rate of light absorption by the irradiated blood vessels should be done.

46.5 Side Effects and Contraindications of ILIB

There is no information about the side effects of ILIB in the literature. However, the contraindications of laser therapy should be considered for ILIB, specially the use of laser without diagnosis, in blood tumor, on pregnant women, and in the pre-surgery period (ILIB can increase bleeding).

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