Photobiological Principles of Therapeutic Applications of Laser Radiation

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Yu. A. Vladimirov, A. N. Osipov, and G. I. Klebanov

FROM ABSTRACT:

Laser therapy is based on the stimulating and healing action of low-intensity lasers (LIL), and has been lately widely applied in the irradiation of human tissues in the absence of exogenous photosensitizers.

Low-intensity lasers photostimulation depends on the radiation wavelength, dose, and distribution of light intensity.

THESE AUTHORS ALSO NOTE:

"The action of visible light on the specialized cells of the eye underlies sight."

Lasers are sources of intense visible and infrared radiation.

The activation of life processes under laser radiation is called "biostimulation."

The positive action of laser biostimulation is changed "into inhibition of vital activity processes" under large doses of laser radiation, "which is a main hindrance to a successful application of laser therapy and a cause of disappointment." **[Very Important: too much or too strong of laser can be deleterious to vital processes].**

Radiation by low-intensity lasers is widely used by "physical therapists and dentists (to reduce pain), dermatologists (treatment of edema, eczema, and dermatitis), surgeons (treatment of persisting ulcers, burns, diabetic foot), rheumatologists (either to relieve pain or treat chronic diseases--arthritis and arthrosis), therapists in veterinary medicine, sports medicine, and rehabilitation centers."

1700 to 2400 papers on therapeutic application of lasers have been published annually during the last ten years, and this number growing steadily.

"The most effective irradiation is that in the red and near infrared range of the spectrum."

"The most commonly used sources are the helium-neon laser (He-Ne) (radiation at 632.8 nm), the gallium-aluminum laser (Ga-Al) (630-685 nm), the helium-neon-arsenate laser (He-Ne-As) (780-870 nm), and the gallium-arsenate laser (Ga-As) (904 nm), as well as light emitting diodes whose emission band lies in a wide region of the spectrum (670 to 950 nm)."

"The main reason for using the sources radiating in the red and near infrared spectral region is the fact that hemoglobin does not absorb in this region and light can penetrate deep into living tissue."

Laser radiation with wavelength of 400 - 500 nm and about 600 nm accelerated cell division in various microorganisms and enhanced protein synthesis.

Laser radiation of fibroblasts with a 632.8 nm laser for 15 minutes accelerates their growth and attachment of cells to substrate, and increased mitotic activity on the 3rd and 4th day after irradiation.

A reliable increase of the mitotic index was also observed after a single radiation of retina epithelium cells with a 632.8 nm laser for 10 min.

"Generally, an expressed extreme relationship between the stimulating action of laser radiation and dose is observed."

Laser radiation of liver mitochondria with a 632.8 nm laser brought about enhanced ATP-ADP metabolism, an increased content of ATP, and morphological changes in the mitochondria.

Laser radiation of blood vessels causes immediate vasodilatation resulting in the "improvement of microcirculation and blood supply in organs."

"Thus, the effects observed in clinic--the antiinflammatory action of laser radiation, an accelerated regeneration of damaged tissues, and the improvement of blood circulation in organs--can be associated with the lasers' effects obtained in experiments:
1) Growth of the activity of certain cells such as leukocytes and phagocytes, as well as an increased content of calcium ions in the cytoplasm of these cells;
2) Enhancement of cell division and cell growth;
3) Activation of the synthesis of proteins and cytokines, and
4) Improvement of blood circulation in the bloodstream due to the relaxation of vessel walls (vasodilatation)."

There exist a great number of hypotheses of possible mechanisms of laser radiation. They can be divided into two categories:

1. Hypotheses based on the idea of a specific action of *coherent (laser) radiation* on human and animal tissues, biological structures as a whole, water structure, etc.

2. Hypotheses of *the photochemical action of light*, including the radiation of lasers, LEDs, and other sources of visible and near infrared light. Karu noted the following hypotheses concerning the mechanism of action of laser radiation.

There are 2 historic theories for the mechanism of laser radiation:

1) The "*singlet oxygen*" hypothesis, according to which the light-absorbing molecules such as porphyrins and flavoproteins can be changed in the respiratory chain of mitochondria into compounds possessing the properties of photosensitizers. Under the action of laser light, these compounds evolve singlet oxygen that can stimulate the synthesis of RNA and DNA.

2) The hypothesis of laser light action on the *oxidation-reduction properties of electron carriers* influences the oxidation-reduction state and, consequently, the electron transfer rate in the molecule, and therefore the production of ATP.

The are 3 newer theories for the biological action of visible light laser radiation:
1) A photodynamic action on membranes accompanied by intracellular calcium increase and cell stimulation;
2) A photoreactivation of Cu-Zn superoxide dismutase; and
3) A photolysis of the metal complexes of NO with release of this vasodilator.

These "three effects underlie the indirect bactericidal, regenerative, and vasodilatation action of laser radiation."

ACCELERATED WOUND HEALING ON LASER IRRADIATION

The phenomenon of photoreactivation of cellular superoxide dismutase (Cu-Zn-SOD) was discovered as the result of the analysis of the data obtained in studies of the action of the 632.8 nm laser on wound healing.

A positive action of laser radiation is observed when using it for treatment of persistent wounds and trophic ulcers; radiation of wounds with a 632.8 nm laser resulted in accelerated wound healing. "Probably, it is partially associated with the intensification of antiradical protection in the wound area."

"Laser radiation increases wound production of hydrogen peroxide." This suggests that laser radiation increases the activity [or production] of the antioxidant enzyme superoxide dismutase, which converts the very harmful superoxide free radical into hydrogen peroxide. [Hydrogen peroxide then helps to sterilize the wound.]

The laser radiation then increases the activity [or production] of the antioxidant enzyme catalase and glutathione peroxidase, which converts residual hydrogen peroxide into water and oxygen.

A mechanism suggested by these authors is that the laser radiation reactivated the activity of catalase or superoxide dismutase enzymes. Both superoxide dismutase and catalase enzymes absorb at the laser light wavelength of 633 nm. **[Important]**

Superoxide dismutase (SOD) requires copper (Cu) and zinc (Zn) to effectively detoxify the superoxide free radical. [together known as Cu-Zn-SOD].

A decreased pH below 5.9 inactivates the superoxide dismutase enzyme, but its complete reactivation was observed under subsequent irradiation with a 632.8 nm laser.

The superoxide free radical is constantly formed during normal metabolism. Higher levels of superoxide free radical are produced under pathologic conditions. The superoxide free radical is toxic for cells and tissues.
The antioxidant enzyme superoxide dismutase (SOD) reduces the concentration of superoxide radical, converting it to hydrogen peroxide and oxygen. If superoxide dismutase levels are low, the cells are injured.

Hydrogen peroxide (produced by the action of the antioxidant enzyme superoxide dismutase) is also a free radical. But, it is a paradoxical free radical. It is a good free radical because it is bactericidal, killing pathogens. However, too much hydrogen peroxide produces the dangerous hydroxyl free radical.

Excess free radical hydrogen peroxide is converted into water and oxygen by the antioxidant enzymes catalase and glutathione peroxidase. [Glutathione requires the trace mineral selenium to effectively detoxify the free radical hydrogen peroxide].

If the superoxide free radical is not detoxified by the superoxide dismutase conversion to hydrogen peroxide, it is converted into three other new and very toxic free radicals when iron is present [remember, excess iron is very toxic because of this mechanism].

The hydroxyl radical, which is highly reactive, brings about the denaturation of protein, and "its reactions with nucleic acids are accompanied by mutagenic and lethal effects."

Another harmful action of superoxide radical it's interaction with nitric oxide NO, which actively forms peroxynitrite-anion. Peroxynitrite has an extremely potent cytotoxic effect. Removing one of the components of the reaction of peroxynitrite formation with SOD protects tissues from damage and prevents destruction, reducing cell damage in many pathological states.

Oxygen deficiency to the brain and/or heart results in damage. Theoretically, restoration of blood circulation should decrease or prevent damage to cells and tissues suffering oxygen deficiency. However, studies show that oxygen reperfusion in these cases may cause additional damage to tissue (*reoxygenation damage*). This is because oxygen reperfusion increases oxygen, drastically increasing the production of superoxide free radical. The superoxide free radical further damages these vital tissues. "Introduction of superoxide dismutase into the perfusion liquid reduces this effect significantly; thus, it can be concluded that it is

free radicals that are mainly responsible for the reoxygenation damage to tissue." Again, the benefits from adding superoxide dismutase is further enhanced with the utilization of laser light therapy.

ACTIVATION OF PROTEIN SYNTHESIS

"An immediate biological consequence of prestimulation of leukocytes (granulocytes and monocytes) by laser irradiation of blood is activation of phagocytosis, i.e., the destruction of bacteria and fungi by these cells." [This is known as the innate immune response].

"Laser irradiation of cells was able to induce the synthesis of a number of proteins," including superoxide dismutase.

"Therefore, a beneficial action of laser irradiation is the result of initiation of primary, free-radical reactions inducing activation of cells (leukocytes, fibroblasts, keratinocytes, etc.) which is expressed in increased bactericidal activity, production of proteins and cytokines, and cell proliferation. All these events are the basis of the therapeutic action of laser therapy."

Laser mechanisms and clinical effects include:

1) Increased protein synthesis.

2) Increased bactericidal activity.

3) Activation of cell proliferation.

4) Accelerated and improved wound healing.

5) Improvement of blood microcirculation.

6) Regeneration of tissues.

7) Improved immunomodulation.

A third hypothesis of the possible mechanism of action of a low-intensity laser radiation increases the release of free nitrous oxide (NO).
[Nitric oxide dilates blood vessels, thus reducing blood pressure and the risk of angina, congestive heart failure, and heart attack.]

ACTIVATION OF ELECTRON TRANSFER IN MITOCHONDRIA UNDER LASER IRRADIATION

Laser radiation of liver mitochondria with 632.8 nm laser light resulted in an increase in the content of ATP, transmembrane potential, and changes in the ultrastructure of organelles. "All these observations suggest the improvement of

respiratory chain functioning. An increased level of ATP in cells was observed also after irradiation of human blood lymphocytes with the light of an infrared (diode) laser at radiation wavelength of 820 nm. These changes in mitochondria indicate the preparation of the cell for division."

"Mitochondrial respiration in the absence of light is partially suppressed by nitric oxide synthesized by mitochondrial NO-synthase. Nitric oxide inhibits respiration due to binding with such electron carriers as cytochromes and cytochrome oxidase, and possibly iron-sulfur complexes. Irradiation by intense light brings about the photolysis of these complexes and restoration of respiration and ATP synthesis."

Therefore, the beneficial action of the low-intensity laser light is based on different primary photochemical reactions, several of which can be considered proved:

1) Photoreactivation of Cu-Zn-superoxide dismutase inactivated at low pH or in hypoxia.

3) Photolysis of mitochondrial membrane complexes of metal-containing proteins with nitric oxide which brings about the release of free NO and reactivation of respiration carriers. When NO is released, it functions as a vasodilator, improving blood flow, which is good. When NO is cleaved from the mitochondrial membrane electron carrier proteins, they become more efficient at producing ATP, which is also good.

"Laser radiation at low doses makes a stimulating effect on cells, and that at high doses a damaging one." **[Very Important]**

KEY POINTS FROM DAN MURPHY:

1) Laser therapy is based on the stimulating and healing action of low-intensity lasers.

2) Too much or too strong of laser can be deleterious to vital processes, and become a "hindrance to a successful application of laser therapy and a cause of disappointment."

3) Low-intensity lasers are used to reduce pain, to treat edema, eczema, dermatitis, persisting ulcers, burns, diabetic foot, arthritis and sports rehabilitation.

4) A 632.8 nm laser increases the content of ATP and causes morphological changes in the mitochondria.

5) Laser radiation of blood vessels causes immediate vasodilatation resulting in the "improvement of microcirculation and blood supply in organs."

6) The newest theory for the biological action of visible light laser radiation is a photoreactivation of Cu-Zn superoxide dismutase anti-oxidant enzyme.

7) The photoreactivation of cellular superoxide dismutase (Cu-Zn-SOD) with a 632.8 nm laser results in accelerated wound healing.

8) Low-intensity laser radiation also increases the activity or production of the antioxidant enzyme catalase and glutathione peroxidase, which converts residual hydrogen peroxide into water and oxygen.

9) Laser radiation reactivates the activity of the antioxidant enzymes catalase and superoxide dismutase. Both superoxide dismutase and catalase enzymes absorb at the laser light wavelength of 633 nm.

10) Superoxide dismutase (SOD) requires copper (Cu) and zinc (Zn) to effectively detoxify the superoxide free radical.

11) The superoxide free radical is constantly formed during normal metabolism. The superoxide free radical is toxic for cells and tissues. The antioxidant enzyme superoxide dismutase (SOD) reduces the concentration of superoxide radical, converting it to hydrogen peroxide and oxygen. If superoxide dismutase levels are low, the cells are injured. Low-intensity laser increases levels of superoxide dismutase.

12) The hydrogen peroxide produced by the action of the antioxidant enzyme superoxide dismutase is also a free radical. But, it is a paradoxical free radical. It is a good free radical because it is bactericidal, killing pathogens. However, too much hydrogen peroxide produces the dangerous hydroxyl free radical. Hydrogen peroxide is converted to water and oxygen by the enzymes catalase and glutathione peroxidase. Low intensity laser increases levels of these two important antioxidant enzymes.

13) Excess free radical hydrogen peroxide is converted into water and oxygen by the antioxidant enzymes catalase and glutathione peroxidase. [Glutathione requires the trace mineral selenium to effectively detoxify the free radical hydrogen peroxide].

14) Other observed effects and mechanisms of low-intensity laser include:
A)) Increased protein synthesis.
B)) Increased bactericidal activity.
C)) Activation of cell proliferation.
D)) Accelerated and improved wound healing.
E)) Improvement of blood microcirculation.
F)) Regeneration of tissues.
G)) Improved immunomodulation.

H)) They are anti-inflammatory.

15) "Laser radiation at low doses makes a stimulating effect on cells, and that at high doses a damaging one." **[Very Important]**

NOTE FROM DAN MURPHY

I have 4 lasers. My favorite is the 635 nm line (not dot) laser from Erchonia. It has 8 laser beams, programmable to 100,000 frequencies, with enough power to get the job done without risking damage: (480) 633-3129 or (888) 242-0571.

		O_2 Oxygen →		Krebs Cycle		
		↓		↓		
Hydroxyl Free Radical OH^- ←	With Iron, Fe	5% Superoxide Free Radical $\cdot O^-_2$		Electron Transport System →		Genesis Of ATP 95%
Superoxide Dismutase 1) w/ Zn 2) w/ Cu 3) w/ Mn (mitochondria) →		↓				
	AND Water H_2O	Hydrogen Peroxide H_2O_2 →		Bactericidal		
		↓				
Catalase →		↓	←	Glutathione Peroxidase (selenium)		
		Water + Oxygen $H_2O + O_2$				

ADDITIONAL COMMENTS FROM DAN MURPHY

Again, there is good evidence that low-level laser therapy works in part because they upregulate (increase the activity of) the genes that produce the three endogenous antioxidant enzymes, superoxide dismutase, glutathione peroxidase and catalase.

Equally importantly, the endogenous antioxidant enzymes require minerals to effectively neutralize destructive free radicals.
Superoxide dismutase requires Zinc, Copper, Manganese.
Glutathione peroxidase requires Selenium.

The incredible effectiveness of low-level laser therapy is further enhanced by supplementing with a balance of zinc, copper, manganese, selenium, and riboflavin (which recharges depleted glutathione). Such a product has been developed by Nutri-West. It is called **LazerMin**. **Laser Minerals** can also be topically applied to the skin with the Nutri-West product **Lazer Ice**. **Nutri-West's** phone number is **(800) 443-3333.**