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MECHANISMS AND EFFECTS OF LOW ENERGY He-Ne LASERS RADIATION ON CIRCULATING BLOOD

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Abstract. The striking effects of intravascular laser blood radiation (ILBR) while treatment of various disease and absence of common conception of its mechanisms compelled to generalize literary data and results of our own studies as a representation of logically completed hypothesis. There has been established the primary acceptor of light influence, its arrangement, conditions of existence and participation in biochemical reactions having the organism response.

While solving the problem concerning ILBR mechanisms, it should be paid greater attention to the characteristic of rather widely interpreted question of registered response in laboratory conditions to the influence of the quantum of energy, and namely: the state of peroxide oxidation of lipoids (POL); the state of antioxidant activity (AOA); the state of immunologic status of an examinee^(1,2).

According to the up-to-date ideas, POL is of great importance in manifestation and course of different pathologic processes. In fact, the POL product level growth leads to the initiation of the chain free-radical oxidation of membrane lipoids and blood plasma lipoproteids affecting the electrochemical potential and the integrity of the cell membrane provoking the change of its immunocompetency. The change of the POL cell and its membrane, in particular, increases enzymic and non-enzymic AOA. In conditions of growing AOA stimulation, the normalization of the maloxidant POL product content is marked, there is a tendency to the increase of non-specific immune protection, the proliferative cell activity increases, the activation of oxidation-reduction processes occurs in the place of pathologic focus, rheological properties of blood become improved, i.e. the optimal conditions for reduction of the normal system functioning are created in this case.

One of the starting-moments of the estimation of the effector response of the studied systems is, undoubtedly, the rule of the datum level formulated by Vilder which is acceptable for the model under investigation. In fact, physiologic "rest" and a number of states of prepathology and pathology are related to the categories of the metastable systems. Just that very fact may serve as a key moment of explanation of the so-called "avalanche-formed" response, up to the marked clinical effects to the minimum external action of physical character, as it may seem. In the given paper laser radiation of low energy plants He-Ne with $\lambda = 0,63$ mmk, He-Cd with $\lambda = 0,44$ mkm, Cu with $\lambda = 0,58$ mkm is used as a test load and in some case as a medical one.

The determination of primary acceptors of incident radiation and the place of its localization is considered to be the basis when estimating the mechanisms of ILBR therapeutic action, as the sequence of photobiological processes with effects of the cellular and organism level depends on this. While solving this problem it's necessary to determine "spectra of action", i.e. the value dependence investigation of any biological effect upon the wavelength. Some authors have found the spectra of action of laser radiation to living organisms that used as a measured value such factors as: the synthesis rate of DNA and RNA in cells Hela; the rate of the culture growth of E. Coly⁽³⁾; the rate of formation of E-rosella-formed cell of human blood lymphocytes; the rate of the L culture division and excretion of DNA-factor by lymphocytes of mice lymphatic nodules⁽⁴⁾.

The maxima at the wavelength of 400–415 nm and 620–630 nm are registered in spectra of action irrespective of dependence upon the object under study. For obtaining the effector response either light intensity or radiation dose in a blue region of spectrum, as a rule, is one order less than that of the

red region (3,5). The analysis of photosensitivity of different cells-prokaryot, primitive and complex-eukaryot allowed T. Karu (1982) to conclude about belonging of primary photoacceptors of the cell oxidation-reduction chain. Here, the quantum absorption by primary photoacceptors causes signal changes in a cell leading to the activation of synthetic processes and after all to the acceleration of the cell growth and division that is one more confirmation of ILBR role in proliferative activity regulation.

Flavin dehydrogenases, cytochromes and many others belong to concrete photoacceptors of biological structure. N. F. Gamaleya (1979) thinks that light is absorbed by some phytochrome system of a living organism as its vegetative analog (6).

As the spectra of action of various biological effects are similar to the absorption spectra of porphyrinic compounds, one may assume that just these very compounds of this group are light receptors in hypothetical system of photoregulation of animal cell (4,7).

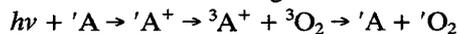
The analogous conclusions about the primary photoacceptor are made in paper by S. M. Zubkov (1978) where there is used porphyrin enzyme-catalase having its absorption maximum in the range of 628 nm, and in paper by Pluzhnikov et al. (1988) copper-bearing enzyme-superoxiddismutase having a low absorption band in the range of 630 nm (8,9). From our point of view, the most valid conclusion belong to R. V. Ambartzumian (1987), who studied them using the investigation data of the action spectra of the region 0,4-0,9 mkm and their comparison with absorption spectra of O₂-molecules in favour of O₂ as a primary photoacceptor (10). This hypothesis has found the additional confirmation in papers by S. D. Zaharov (1988, 1989), where the spectrum of action of IR radiation in the region of the so-called atmospheric adsorption line O₂Σ - 'Δ with λ = 1,26 mkm with the help of the tuned diode laser (11,12). In this paper the value of the membrane deformity, and namely: T_{max}⁻¹ of erythrocytes, which was inverse to time of maximum progress was taken as a measured parameter. As a result, there has been obtained almost complete coincidence of the absorption line contour O₂ with a biological response of erythrocyte membranes to the wavelength. However there are two important facts that complicate the choice of the molecule O₂ as a primary acceptor of photons and a leading component element in initiation of free-radical oxidation.

Firstly, due to radiation veto to transitions with a variation of spin and orbital quantum numbers, the excitation section of molecules O₂ with photon from the fundamental state ³Σ_g into excited singlet one 'Δ and 'Σ makes up a small value equal to σ ~ 10⁻²⁴ cm² (12).

Secondly, the life time of singlet O₂ in cytoplasm of cells is negligible and makes up only ~ 10⁻⁹-10⁻¹¹ s due to energy degradation of election excitation of state 'Δ and 'Σ at physical collision with molecular components of a cell as well as the use of this energy in chemical transformations (13).

Both these moments testify to the fact that the total concentration of excited free oxygen is extremely small, so the probability of its initiation of biological consequences on the cellular and organism level connected with excited O₂ is hardly real. At the same time, there is lost the fact that radiation ban with spin variation is removed in high electric fields that exist within membranes of a living cell. This estimation explains the fact that in the fields which exist in membranes of a living cell equal to ~ 10⁵ V/cm, the absorption section of photons may increase up to 4-5 orders, i.e. make up a value 10⁻¹⁹-10⁻²⁰ cm². At the same time, oxygen having a small solubility in water tends to localizations in places not occupied with water. To such places one may relate the intervals of the cell membrane formed by hydrophobic ends of lipoids. In this case the molecular ³O₂ transferring to the excited state 'O₂ under the influence of laser radiation, has possibility to enter directly into chemical interaction with membrane of lipoids.

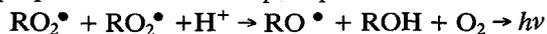
Of course, the above-stated does not exclude that molecular O₂ may be excited by means of exogenous and endogenous photosensitizers according to the reaction:



the more so as in interlipoid space there is a great number of ferruginous molecules including cytochromes.

If one may assume that the main light acceptor are O₂-molecules being in interlipoid membrane space, then immediately after excitation into a singlet state the molecule of 'O₂ "attacks" the hydrophobic ends of lipoids - RH, e.g., lipoic or linolic acid breaking double bonds of non-saturated fatty acids (NFA). Appearing here the lipid peroxide ROOH in the presence of reduced forms Fe⁺² or other reduced components of a cell (ascorbic acid, cystein, glutatione, NADP and NADH), capable of the interaction with Fe⁺³, initiates the chain reaction PNFA of the cell and blood plasm (14).

The presence of peroxide radicals of lipoids may be found using the data of chemoluminescence caused by reaction of disproportionation of the lipid peroxide radicals:



Here, the concentration of RO_2^* decreases breaking the chains of POL. In addition to the mechanism of POL chain breaking, caused by recombination reactions of radicals, the POL process is regulated by means of AOA of various antioxidants (α -tocopherol, indole and the like) as well as by hydroperoxide neutralisation connected with fermentative oxidation of reduced glutathione (GSH):



where GSH is a glutathione peroxidase.

The POL process according to standard is subjected to the strict control on the part of an organism, however, different pathologic processes may lead to AOA decrease in tissues or to breaking of structural membrane barriers that, in its turn, may accelerate significantly the POL process. The POL intensity, as it was shown above, may increase abruptly also in case of initiation of chain processes of NFA oxidation. The formation of lipid peroxides changes the membrane permeability due to the process of oxidation of the non-saturated hydrophobic "tails" of phospholipids. The hydroperoxide groups obtained as a result, cause the appearance of "holes" in hydrophobic barrier of the cell membrane⁽¹⁵⁾. The active transport of Na^+ and K^+ ions is broken⁽¹⁶⁾. In parallels there is noted the increase of passive cation transport through abluminous canals⁽¹⁷⁾. The above-mentioned statements lead to the fact concerning the transmembrane Na^+ and K^+ exchange (1:1) without changing the volume of a cell. After the output of 80 % of K^+ ion from the cell, the input of Na^+ begins to exceed the output of K^+ and as a result, some water is put into the cell and osmotic lysis takes place here⁽¹⁸⁾. However, even at the first stages of this process the regulation of proliferative cell activity as a result of interaction between POL and AOA may be possible, i.e. the cell division of the reproductive age^(19, 20).

Thus we have approached closely to the understanding of the purposeful selection of the wavelength of the emitter taking into account the action spectra and the absorption bands of a hypothetic light acceptor by the estimation of the starting mechanisms of registered clinical effects of laser radiation of a pathologic focus as well as a particular case of ILRB.

In this paper we have considered the points of applications of the studied laser emitters. The correspondence of the action spectra to the total absorption spectra of oxygen for a He-Cd laser and separate peaks for Cu and He-Ne lasers is shown rather clear that is considered to be the facts confirming our conception.

The important aspect in explanation of picture of the effector organism response to minimum external influence (as it may seem) is a question concerning the sufficient initiation of the process of free-radical PNFA oxidation. In fact, using the wavelength of a laser emitter approximating to maxima of the absorption spectrum of the whole blood, it is practically impossible to achieve effects concerning ILRB on account of the use of minimum volumes of a flowing blood that has obtained the laser pumping. The attenuation of light transmission by venous blood is determined by the following: on the short-wave side-by scattering processes of radiation in heterogeneous medium and by hemoglobin absorption, and on the long-wave side-by water absorption. The obtained result of light transmission of the whole blood is a determination of a maximum in the range of about ~ 925 nm. Taking into account this fact, it should be paid greater attention to the investigation prospects of the given region concerning the wavelength in a volume of elaborations devoted to optic monitoring of internal organs and systems. The absence of clinical effects of the use of the Cu laser radiation effect for ILRB and the presence of the same while the beam action with $\lambda = 0,58$ mkm directly to the pathologic focus is explained by the marked attenuation of light transmission. In spite of the fact, that the wavelength of a He-Ne laser equal to 630 nm does not correspond to the region of maximum light transmission of the whole blood, it is sufficient for blood volume radiation in a vascular bed with a diameter up to 1-1,5 cm (i.e. a cubital vein and arranged closely vessels of the venous and arterial system). While duration of exposure equal to 30 minutes, the preliminary calculations give the possibility to make sure of it for single and double radiation of the whole volume of quick-circulating or active-circulating blood of a patient having weight of 65-75 kg⁽²¹⁾.

Thus summing it up, it should be stressed the following aspects:

- taking into account the data of the spectra of the biological action, the main primary light acceptor is free oxygen that while photon absorption of electromagnetic laser radiation is excited from the basic state $^3\Sigma$ into singlet states $^1\Sigma$ and $^1\Delta$ with high reactivity. This way does not exclude the possibility of the singlet oxygen formation through the action of endogenous photosensitises;
- the main biological consequences are caused by singlet oxygen which is localized in interlipid region of the cell membrane;
- the excited oxygen initiating the chain reactions of peroxide oxidation of NFA lipoids leads to the permeability change of the membrane and increase of passive ion transport, causing either proliferation

(depending on the process manifestation) or the osmotic breaking of a cell while reaching some critical values of the electrochemical potential of membranes $\Delta\mu$;

- the effects of the intravascular laser radiation of blood are closely connected with a wave characteristic of applied laser emitter and should correspond to the light transmission spectrum of the whole blood as well as to the action spectrum of O₂ molecules.

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