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Photobiomodulation—Rapid Communication

Photobiomodulation: Shining Light on COVID-19

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Abstract

Objective: To evaluate the hypothesis that light could reduce the lethality of COVID-19.
Methods: Most models for projections of the spread and lethality of COVID-19 take into account the ambient temperature, neglecting light. Recent advances in understanding the mechanism of action of COVID-19 have shown that it causes a systemic infection that significantly affects the hematopoietic system and hemostasis, factors extremely dependent of light, mainly in the region of visible and infrared radiation.
Results: In the COVID-19 patients hemoglobin is decreasing and protoporphyrin is increasing, generating an extremely harmful accumulation of iron ions in the bloodstream, which are able to induce an intense inflammatory process in the body with a consequent increase in C-reactive protein and albumin. Observing the unsaturation characteristics of the cyclic porphyrin ring allows it to absorb and emit radiation mainly in the visible region. This characteristic can represent an important differential to change this process in the event of an imbalance in this system, through the photobiomodulation to increase the production of adenosine triphosphate (ATP) using red and near-infrared radiation (R-NIR) and vitamin D using ultraviolet B (UVB) radiation. These two compounds have the primary role of activating the defense mechanisms of the immune system, enabling greater resistance of the individual against the attack by the virus. According to the theory of electron excitation in photosensitive molecules, similar to hemoglobin heme, after the photon absorption there would be an increase in the stability of the iron ion bond with the center of the pyrrole ring, preventing the losses of heme function oxygen transport (HbO_2). The light is also absorbed by cytochrome c oxidase in the R-NIR region, with a consequent increase in electron transport, regulating enzyme activity and resulting in a significant increase of oxygen rate consumption by mitochondria, increasing ATP production.
Conclusions: The most favorable range of optical radiation to operate in this system is between R-NIR region, in which cytochrome c oxidase and porphyrin present absorption peaks centered at 640 nm and HbO_2 with absorption peak centered at 900 nm. Based on the mechanisms described earlier, our hypothesis is that light could reduce the lethality of COVID-19.

Keywords: photobiomodulation, light, COVID-19

Recent advances in understanding the mechanism of action of COVID-19 have shown that it causes a systemic infection that significantly affects the hematopoietic system and hemostasis.[1] Chen et al.[2] evaluated biochemical tests of patients with pneumonia caused by coronavirus and their biochemical data revealed that the hemoglobin and neutrophil counts of most patients decreased, whereas the serum ferritin, erythrocyte sedimentation rate, C-reactive protein, albumin, and lactate dehydrogenase in many patients increased significantly. Thus, the patient's hemoglobin is decreasing and protoporphyrin is increasing, generating an extremely harmful accumulation of iron ions in the bloodstream, which are able to induce an intense inflammatory process in the body.[3]

Liu and Li[3] compared the biological roles of certain proteins in the new coronavirus. The results obtained by these authors showed that ORF8 and viral surface glycoprotein can bind to porphyrin. In addition, the orf1ab, ORF10, and ORF3a proteins can coordinate the heme attack on the hemoglobin beta-1 chain to dissociate iron and thus form protoporphyrin. Hence, hemoglobin would lose its ability to transport oxygen and carbon dioxide. In turn, the lung cells have reduced gas exchange capacity (CO_2 and O_2) along with an intense and acute inflammatory process. The transport of compromised oxygen induces hypoxia, which may be the reason why many patients even assisted with supplemental oxygen

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therapy do not present a favorable evolution of their clinical condition.

The unsaturation characteristics of the cyclic porphyrin ring allow it to absorb and emit radiation mainly in the visible region. This characteristic can represent an important differential to change this process in the event of an imbalance in this system, through the absorption of light to produce therapy, or to assess its dynamics, through the emission of light, allowing a diagnosis to be made.

The theory of electron excitation in photosensitive molecules[4] and observed characteristics of the hemoglobin heme molecule after the absorption of a photon indicate that the electrons attached to the heme molecule are excited, altering the distribution of its electronic density and facilitating the transfer of electrons.[5] This would increase the stability of the iron ion bond with the center of the pyrrolic ring, preventing the heme from losing its oxygen transport function. In parallel, light is also absorbed by cytochrome c oxidase in the red and near-infrared radiation (R-NIR) region, with a consequent increase in electron transport, regulating enzyme activity and resulting in a significant increase in the rate of oxygen consumption in tissue mitochondria,[6] increasing adenosine triphosphate (ATP) production by this process.

Vitamin D absorbs UVB radiation at wavelengths between 290 and 315 nm and this process is essential for this activation. Vitamin D increases innate cellular immunity, partially by inducing antimicrobial peptides, including human cathelicidin LL-37, from 1,25-dihydroxyvitamin D[7,8] and defensins.[9] Cathelicidins present antimicrobial activity against a wide spectrum of microorganisms, including Gram-positive and Gram-negative bacteria, virus and fungi.[10] Grant et al.[11] presented evidence that vitamin D supplementation could reduce risk of deaths and COVID-19 infections. Study employed global data discovered a strong correlation between vitamin D deficiency and COVID-19 mortality rates.[12] These two compounds, ATP and vitamin D, have the primary role of activating the defense mechanisms of the immune system, enabling greater resistance of the individual against the attack by the virus.

UVB is absorbed superficially in the epidermis, once that the activation of vitamin D occurs in the stratum corneum of the skin.[13] In this case the most favorable wavelength to irradiate porphyrin is in the red region,[14,15] because the blood circulation porphyrins, our principal target presents better absorption in this region due to the higher tissue penetration if compared with UVB.

Two options are more suitable to irradiate these molecules, one acting in the red region, in which cytochrome c oxidase and porphyrin present absorption peaks centered at 640 nm-$\lambda1$ and another in the NIR region, in which the peak absorption of HbO_2 is centered on 900 nm-$\lambda2$ (Fig. 1).

Considering the strengthening of the iron ion bond with the center of porphyrin pyrrolic rings, the two wavelengths are interesting, $\lambda1$ acting directly on the porphyrin molecule and $\lambda2$ on the HbO_2 molecule. This may also strengthen the immune system, with $\lambda1$ acting on cytochrome c oxidase to increase ATP production and $\lambda2$ acting on cell membrane permeability to increase the flow of intracellular calcium with a consequent increase in vitamin D. However, recent studies present a different hypothesis for the increase in ATP synthesis by irradiated mitochondria. According to the authors, the major cause for light-induced upregulation of mitochondrial ATP is not related to absorption by cytochrome c oxidase, but a physical process involving a decrease in interfacial water layer viscosity in the irradiated mitochondria. This information could justify the fact that mitochondrial ATP synthesis can be stimulated by different wavelengths of LED and laser.[16,17]

Based on this premise, and partial results obtained by our research group with patients exhibiting bacterial pneumonia, for which we obtained a reduction in hospital stay from 7 to 2 days, for 9 out of 10 treated patients.[18] We propose to treat patients affected by COVID-19 irradiating their thoracic region daily with R-NIR, with 3 J/cm^2 of radiant exposure. Patients using this device would be those in an intermediate, semicritical, and critical state. Patients who present with porphyrias would use this device emitting only radiation in the NIR, thus preventing the photobiomodulation of protoporphyrins, which in this case, because they are present in large numbers in the bloodstream, could cause skin burns.

A recent study on COVID-19 evidenced that high temperature (up to 21°C) reduce the transmission of COVID-19 with 1% significance levels.[19] Another factor to be considered in this way, which has not been taken into account in the projections of the spread and lethality of the virus, is the presence of light. Naturally, a higher incidence of light on the Earth's surface in a given region is directly related to

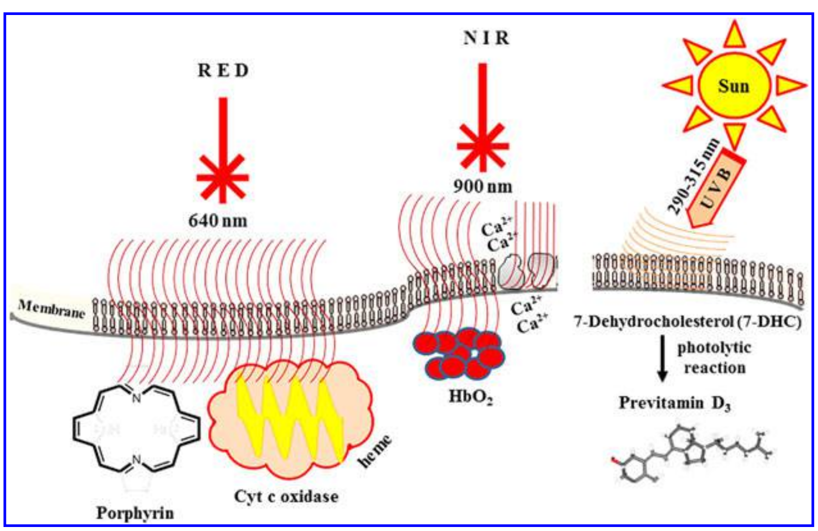

FIG. 1. Photobiomodulation mechanisms.

an increase in the ambient temperature of that region. Nevertheless, but these two variables, although related, are independent and can assume important roles in the study of the dissemination and lethality of COVID-19. Based on the mechanisms described earlier, our hypothesis is that light plays a major role in reducing the lethality of COVID-19.

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